APPENDIX C

Evaluating Potential Risks to Infants from Consuming Human Milk

INTRODUCTION

This appendix presents a standard approach for evaluating potential risks to infants from consumption of human milk. The approach was developed in conjunction with EPA Region 10 risk assessors. The following is consistent with the approach recommended by EPA, and with Oregon Administrative Rules.

DEQ evaluated the feasibility of conducting a risk assessment based on exposure to human milk using EPA's *Methodology for Assessing Health Risks Associated with Multiple Pathways of Exposure to Combustor Emissions*[1] (MPE Guidance), *Human Health Risk Assessment Protocol for Hazard Waste Combustion Facilities*[2] (Combustion Guidance), *Exposure Factors Handbook*[3], *Child-Specific Exposure Factors Handbook*[4], and examples from other hazardous waste sites. We determined that it is feasible to include exposure to human milk in human health risk assessments, and that this is an important exposure pathway for bioaccumulating chemicals. Risk assessments for sites contaminated with polychlorinated biphenyls (PCBs), chlorinated dibenzenzo-p-dioxins (CDDs) and chlorinated dibenzofurans (CDFs), and/or DDT compounds (including DDE and DDD) should include potential risks from the breast feeding pathway. Although DEQ considers these chemicals to be the most important contributors to risk from this pathway, we may require that you include other bioaccumulating chemicals released at the facility in your risk assessment.

To assist risk assessors in incorporating the human milk consumption pathway into the human health risk assessment, we prepared this appendix to present relevant exposure and risk equations, and exposure and toxicity parameters (summarized in Tables 1 and 2). We include example calculations using total PCB Aroclors to show how the various equations in EPA's MPE guidance can be modified to focus on fish consumption, one of the most important exposure pathways for bioaccumulating chemicals. However, the general calculations for infants apply to <u>every</u> exposure pathway that the mother may experience prior to and during breastfeeding. Actual risk assessments should include the exposure pathways relevant for the site. Risk assessments should also include all relevant chemicals, such as total PCBs (from Aroclors or congeners), 2,3,7,8-TCDD equivalents (from chlorinated dibenzo-*p*-dioxins, chlorinated dibenzofurans, and dioxin-like PCB congeners, evaluating each chemical class separately and collectively as the sum of all dioxin-like chemicals), and DDT and its degradation products.

The methods discussed in this attachment are appropriate for lipophilic compounds that are present mostly in milkfat rather than the aqueous phase. Equations are also available for compounds that will partition more to the aqueous portion of human milk. Specific guidance for hydrophilic compounds is not presented in this document.

We include relative risk ratios in this appendix (Table 3) so that all the risk calculations for human milk ingestion do not need to be included in risk assessments. Instead, the potential risk to infants can be calculated based on the exposure to the mother, which

should already be evaluated for relevant exposure pathways. This will simplify incorporation of the breast feeding pathway into the risk assessment.

Generally, risk assessments are limited to an evaluation of risk, and do not consider comparative risks or benefits. For example, eating fish is health beneficial compared with eating other animal protein. Public health agencies commonly address the health tradeoffs of eating contaminated fish, but the issue is not typically discussed in a Superfund risk assessment. For breast feeding, however, the benefits to infants are so substantial that we consider it appropriate to discuss the issue in the risk assessment report. The Oregon Environmental Health Assessment Program (EHAP) has prepared a letter that presents the risks and benefits of consuming contaminated human milk. This letter has been reviewed by the Agency for Toxic Substances Control (ATSDR). DEQ recommends that information presented in Attachment 1 be included with risk assessments that include the breast feeding pathway.

PROPOSED RISK ASSESSMENT APPROACH

Exposure Assessment

We mainly relied on the equations presented in EPA's MPE document[1], using a fish ingestion scenario for the mother to illustrate the approach for calculating risk to the breastfeeding infant. The key concept is that the concentration of a chemical in milk can be calculated from the long-term body burden in the mother. This is consistent with the information presented in the Agency for Toxic Substances Disease Registry (ATSDR) *Toxicological Profile for Polychlorinated Biphenyls*[5].

Average Daily Dose to Mother

We start with the average daily intake of chemicals to the mother. The general Equation C-1, modified from Table C-1-4 of the Combustion Guidance[2], is then further modified to consider absorbed dose (Equation C-2) so that body burden in the mother can be estimated.

Equation C-1
General Equation for Average Daily Dose to Mother

$$ADD_{mat} = \frac{C \times CR \times EF \times ED}{AT \times BW_{mat}}$$

Where:

ADD_{mat}	= Average daily dose of chemical to mother (mg/kg/day)
C	= Chemical concentration in medium of interest (e.g., mg/kg in soil)
CR	= Contact rate (e.g., mg/day)
EF	= Exposure frequency (e.g., days/year)
ED	= Expsoure duration (e.g., years)
AT	= Averaging time (70 years = 25550 days for carcinogens, = ED for noncarcinogens)
BW_{mat}	= Body weight of mother (66 kg for average adult female aged 15 to 44)

Equation C-2
Daily Absorbed Intake to Mother

$$DAI_{mat} = ADD_{mat} \times AE_{mat}$$

Where:
DAI_{mat} = Daily maternal absorbed intake of chemical (mg/kg/day)
ADD_{mat} = Average daily dose of chemical to mother (mg/kg/day) Equation C-1
AE_{mat} = Absorption efficiency of chemical (fraction)

For the example exposure evaluated in this appendix, we consider exposure to the mother by consumption of fish contaminated with PCBs:

Equation C-3
Average Daily Dose to Mother from Fish Ingestion

$$ADD_{mat} = \frac{C_{fish} \times IR_{fish} \times CF \times F_{fish}}{BW_{mat}}$$

Where:
ADD_{mat} = Average daily dose of chemical to mother (mg/kg/day)
C_{fish} = Chemical concentration in fish (mg/kg)
IR_{fish} = Ingestion rate of fish for mother (standard default rate of 17.5 g/day)
CF = Conversion factor (0.001 kg/g)
F_{fish} = Fraction of fish contaminated (1)
BW_{mat} = Body weight of mother (66 kg)

The ingestion rate used in the example is the default rate used by EPA in developing ambient water quality criteria. The fish consumption rate is an annualized rate (*i.e.*, it includes the assumption that fish are eaten throughout the year), so exposure frequency, exposure duration, and averaging time are not included in the equation. Loss of chemicals during cooking, which has been considered at other sites, is not included in EPA's Combustion Guidance. However, cooking loss can be addressed in the uncertainty section of a risk assessment. For body weight, we follow recent EPA guidance[8] and consider it appropriate to use the average female weight aged 15 years to 44 years of 66 kg. Prior default values were 70 kg (average adult weight) used in EPA's Combustion Guidance[2], and 60 kg (average female weight) used in EPA's MPE Guidance[1].

For this example, the calculations are performed assuming a total PCB concentration of 1 mg/kg in whole-body tissue. This value is for illustration only, and to develop a relative risk ratio. An actual risk assessment should use chemical concentrations appropriate for the various species of fish sampled.

$$ADD_{mat} = 1 \text{ mg/kg} \times 17.5 \text{ g/day} \times 0.001 \text{ kg/g} \times 1 \ / \ 66 \text{ kg} = 0.000265 \text{ mg/kg/day}$$

Assuming an absorption efficiency of 1 (AE_{mat} in Equation C-2), DAI_{mat} is equal to ADD_{mat}.

Equation C-3 is appropriate for evaluating non-carcinogenic effects to the mother. For an excess lifetime cancer risk calculation for the mother, the equation would be modified to incorporate exposure duration (typically 30 years) and averaging time (lifetime of 70 years). The resulting average daily dose would be reduced by a factor of 30/70, or 0.43 times the ADD calculated above, resulting in a lifetime dose of 0.00011 mg/kg/day.

Chemical Concentration in Milkfat

EPA found that dietary intake of PCBs during pregnancy and lactation is only weakly correlated with PCB concentrations in human milk. The more important determinant is long-term consumption of PCBs. The following simplified equation is an initial approximation to calculate the PCB concentration in milk fat.

Equation C-4
Steady State Chemical Concentration in Milkfat

$$C_{milkfat,ss} = \frac{DAI_{mat} \times h \times f_f}{\ln(2) \times f_{fm}}$$

Where:

$C_{milkfat,ss}$ = Chemical concentration in milkfat (mg/kg-lipid)
DAI_{mat} = Daily absorbed chemical intake to mother (mg/kg/day)
h = Half-life of chemical (days)
f_f = Fraction of absorbed PCB stored in fat (0.9)
f_{fm} = Fraction of mother's weight that is fat (0.3 kg-lipidBW/kg-totalBW)

Equation C-4 was modified from Table C-3-1 of the Combustion Guidance[2], and is consistent with equations 1 through 3(b) in Section 3.4.4.2 of the ATSDR *Toxicological Profile*[5]. The equation is for steady-state conditions, assuming that maternal intake occurs over a time-period greater than the chemical half-life. Another important assumption is that chemical concentrations in human milk reflect the maternal body burden.

For the PCB example, the assumed half-life is 7 years (2555 days) following the Combustion Guidance[2]. The calculated PCB concentration in milkfat is:

$$C_{milkfat,ss} = \frac{0.000265 \text{ mg/kg-totalBW/day} \times 2555 \text{ days} \times 0.9}{0.693 \times 0.3 \text{ (kg-lipidBW/kg-totalBW)}}$$

$$= 2.9 \text{ mg/kg-lipid}$$

In EPA's MPE guidance, a more complex equation is used to explicitly consider two factors relevant to average milkfat concentrations over the time that an infant is breastfeeding. The modified approach avoids overestimating breastmilk concentrations by: 1) estimating maternal body burden at the start of breastfeeding taking into account the exposure period of the mother relative to the metabolic halflife of the chemical, rather than assuming steady-state conditions, and 2) accounting for the reduction in chemical concentrations over time during the breastfeeding period as chemical mass is

transferred from mother to infant. Both of these factors are incorporated into the following equation (taken from Equation 9-4 in MPE guidance[1]).

Equation C-5
Average Chemical Concentration in Milkfat During Breastfeeding

$$C_{milkfat,avg} = \frac{DAI_{mat} \times f_f}{k_{elim} \times f_{fm}} \times \left[\frac{k_{elim}}{k_{elac}} + \frac{1}{k_{elac} \times t_{bf}}\left(1 - e^{-k_{elim}t_{pn}} - \frac{k_{elim}}{k_{elac}}\right)\left(1 - e^{-k_{elac}t_{bf}}\right)\right]$$

Where:

$C_{milkfat,avg}$ = Average chemical concentration in milkfat (mg/kg-lipid)
DAI_{mat} = Daily absorbed chemical intake to mother (mg/kg/day); Equation C-2
f_f = Fraction of ingested chemical stored in fat (0.9)
f_{fm} = Fraction of mother's weight that is fat (0.3 kg-lipidBW/kg-totalBW)
k_{elim} = Elimination rate constant for non-lactating women (days^{-1}); Equation C-6
k_{elac} = Elimination rate constant for chemical in milkfat during breast feeding (days^{-1}); Equation C-7
t_{pn} = Duration of mother's exposure prior to breastfeeding (20 years = 7300 days)
t_{bf} = Duration of breastfeeding (365 days)

The elimination rate constants k_{elim} and k_{fat_elac} are calculated as shown below.

Equation C-6
Biological Elimination Rate Constant for Women Prior to Breastfeeding

$$k_{elim} = \frac{\ln(2)}{h}$$

Where

k_{elim} = Elimination rate constant for non-lactating women
h = Half-life of chemical (days)

Equation C-7
Biological Elimination Rate Constant for Women who are Breastfeeding

$$k_{elac} = k_{elim} + \frac{IR_{milk} \times f_f \times f_{mbm}}{f_{fm} \times BW_{mat}}$$

Where

k_{elac} = Elimination rate constant for chemical in milkfat during breast feeding (days^{-1})
K_{elim} = Elimination rate constant for non-lactating women (days^{-1})
IR_{milk} = Ingestion rate of milk over duration of breast feeding (0.98 kg/day)
BW_{mat} = Body weight (66 kg)

f_f = Fraction of ingested chemical stored in fat (0.9)
f_{mbm} = Fraction of fat in mother's milk (0.04)
f_{fm} = Fraction of mother's weight that is fat (0.3 kg-lipidBW/kg-totalBW)

The first term in Equation C-5 ($DAI_{mat}\ f_f / k_{elim}\ f_m$) is equivalent to Equation C-4, given the definition of k_{elim} in Equation C-6. The other terms in Equation C-5 account for chemical concentrations in the mother prior to steady-state concentrations (if the duration of exposure to the mother is less than about three times the elimination halflife), and also chemical losses during breastfeeding.

In the PCB example, with an assumed half-life of 7 years (2555 days), the calculated rate constants are:

$$k_{elim} = \ln(2) / 2555 \text{ days} = 0.693 / 2555 \text{ days} = 0.00027 \text{ (days)}^{-1}$$

$$k_{elac} = 0.00027 + (0.98 \times 0.9 \times 0.04)/(0.3 \times 66) = 0.0021 \text{ (days)}^{-1}$$

Using these values, the average concentration of PCB in milkfat over a year of breastfeeding calculated from Equation C-5 is:

$$C_{milkfat} = 1.9 \text{ mg/kg-lipid}$$

This more realistic value is similar to the value of 2.9 mg/kg-lipid calculated using simplified Equation C-4.

In order to explicitly evaluate the magnitude of effect of accounting for 1) steady state concentrations not being reached, and 2) chemical loses during breastfeeding, we present a simplified version of Equation C-5 in Attachment 2. For the PCB example, we show that the steady-state maternal concentration (Equation C-4) is reduced by a factor of 0.86 to account for non-steady state conditions, and another factor of 0.70 to account for mass loses during breastfeeding, to calculate a mean PCB concentration in human milk during breastfeeding.

Average Daily Dose to Infant from Milkfat

For lipophilic chemicals such as PCB, the majority of the chemical will be partitioned in milkfat, so once we have calculated $C_{milkfat}$ we can calculate the average daily dose to a breastfeeding infant using the following equation (modified from Equation 9-1 of the MPE Guidance[1]):

Equation C-8
Average Daily Dose to Breastfeeding Infant

$$ADD_{inf} = \frac{C_{milkfat} \times f_{mbm} \times CR_{milk} \times ED_{inf}}{BW_{inf} \times f_{am} \times AT}$$

Where:

ADD_{inf} = Average daily dose to breast-feeding infant (mg/kg/day)
$C_{milkfat}$ = Concentration of chemical in milk fat (mg/kg-lipid)
f_{mbm} = Fraction of fat in mother's milk (0.04)
f_{am} = Fraction of chemical absorbed by the mother (1)
CR_{milk} = Consumption rate of human milk (0.98 kg/day)
ED_{inf} = Exposure duration of breast-feeding infant (365 days)
BW_{inf} = Average body weight of infant over ED (7.8 kg)
AT = Averaging time: carcinogen (70 years x 365 days/year)
non-carcinogen (AT = ED)

Equation 9-1 in EPA's MPE guidance includes the term f_{ai} for fraction of ingested chemical absorbed by the infant. This term was included in the original calculations[6] because infant body burden was used to evaluate risk. However, for typical evaluations of risk using either reference doses or slope factors, we use administered dose, not absorbed dose. Therefore, the term f_{ai} is not included in the calculation of dose to infant in Equation C-8. Note, however, that Equation C-2 does use the fraction of chemical absorbed by the mother (AE_{mat}). This is because $C_{milkfat}$ is based on body burden in the mother, which is dependent on absorbed dose, not administered dose.

For the PCB example, the ADD values for carcinogenic and noncarcinogenic effects are calculated as follows:

$$ADD_{ca\text{-}infant} = \frac{2.9\ mg/kg\text{-}lipid \times 0.04\ kg\text{-}lipid/kg\text{-}milk \times 0.98\ kg/day \times 365\ day/yr}{7.8\ kg \times 1 \times 70\ yr \times 365\ day/yr}$$

$$= 0.00014\ mg/kg/day$$

$$ADD_{nc\text{-}infant} = \frac{2.9\ mg/kg\text{-}lipid \times 0.04\ kg\text{-}lipid/kg\text{-}milk \times 0.98\ kg/day \times 365\ day/yr}{7.8\ kg \times 1 \times 365\ day/yr}$$

$$= 0.0095\ mg/kg/day$$

Aqueous Component

EPA's MPE Guidance includes an approach for evaluating infant exposure to chemicals in the aqueous phase of human milk. The approach presented here in DEQ guidance is limited to lipophilic compounds that are preferentially present in milkfat. We do not anticipate expanding the evaluation to include hydrophilic compounds at this time. If it is determined that this pathway should be included in a risk assessment, the equations in Chapter 9 of EPA's MPE Guidance[1] can be used.

Mercury Exposure

EPA has extended their MPE Guidance with additional information on how to evaluate exposure to mercury in human milk[7]. They refer to a study that showed that methyl mercury concentrations in blood of nursing infants were similar to methyl mercury concentrations in the mothers' blood. EPA concludes that, for the purpose of a risk assessment, the dose of mercury to the infant can be assumed to be approximately

equal to the dose to the mother during breastfeeding. EPA's guidance on risk assessment methodologies[8] can be referred to if mercury exposure is a relevant pathway.

Toxicity Assessment

EPA's hierarchy for selecting toxicity factors is to first obtain factors from EPA's Integrated Risk Information System (IRIS). For example, the cancer slope factor for PCBs presented in IRIS is 2 $(mg/kg/day)^{-1}$. This value is applied to total PCBs.

The RfD for PCBs in IRIS is 2×10^{-5} mg/kg/day for chronic exposure (7 years to lifetime). There is no RfD for subchronic exposure in IRIS. Following EPA's hierarchy for toxicity values, the next source for a subchronic RfD is ATSDR. The ATSDR minimal risk level (MRL, comparable to an RfD) is 3×10^{-5} mg/kg/day for intermediate-duration (subchronic) oral exposure to PCBs. ATSDR defines intermediate-duration exposure as two weeks to one year. The intermediate-duration MRL was derived from a study on monkeys that approximated exposure during breastfeeding using a mixture of PCB congeners typically found in human milk. For this reason, it is a better indicator of toxicity than the chronic RfD (which is equal to the chronic MRL).

Table 1 provides the slope factors, chronic reference doses, and where available, subchronic reference doses for bioaccumulating chemicals.

Risk Characterization

Calculated Cancer Risk to Infants

Using the standard risk characterization equations, excess lifetime cancer risk and non-cancer hazards are calculated separately. Excess lifetime cancer risk is approximated by:

Equation C-9
Calculation of Excess Lifetime Cancer Risk to Breastfeeding Infant

$$ELCR_{infant} = ADD_{ca\text{-}infant} \times SF_o$$

Where:
$ELCR_{infant}$ = Excess lifetime cancer risk to infant from breast feeding
$ADD_{ca\text{-}nfant}$ = Average daily dose (cancer) for breast-feeding infant (mg/kg/day)
SF_o = Cancer slope factor – oral $[(mg/kg/day)^{-1}]$

Using the slope factor of 2 $(mg/kg/day)^{-1}$ for total PCBs, the ELCR for the example is:

$$ELCR_{infant} = 0.00014 \text{ mg/kg/day} \times 2\ (mg/kg/day)^{-1} = 3 \times 10^{-4}$$

Calculated Non-Cancer Risk to Infants

The non-cancer hazard quotient is:

Equation C-10

Calculation of Non-Cancer Hazard Quotient to Breastfeeding Infant

$$HQ_{infant} = \frac{ADD_{nc\text{-}infant}}{RfD}$$

Where:
HQ_{infant} = Hazard quotient for breast-feeding infant
$ADD_{nc\text{-}infant}$ = Average daily dose (non-cancer) for breast-feeding infant (mg/kg/day)
RfD = Non-cancer reference dose (mg/kg/day)

Using the intermediate-duration MRL of 3×10^{-5} mg/kg/day for total PCBs, the calculated hazard quotient is:

$$HQ_{infant} = 0.0095 \text{ mg/kg/day} / 3 \times 10^{-5} \text{ mg/kg/day} = 317$$

Comparative Risk

For comparison, the calculated risks to the mother given the exposure assumptions are the following. For carcinogenic effects, using the long-term ADD and the oral slope factor:

$$ELCR_{mother} = 0.00012 \text{ mg/kg/day} \times 2 \text{ (mg/kg/day)}^{-1} = 2 \times 10^{-4}$$

For noncarcinogenic effects, using ADD without factoring in exposure duration, exposure frequency, and averaging time, and using the chronic reference dose:

$$HQ_{mother} = 0.000265 \text{ mg/kg/day} / 2 \times 10^{-5} \text{ mg/kg/day} = 13$$

The relative ratios of risk to the infant compared with risk to the mother are the following:

$$\text{Cancer Relative Risk Ratio} = ELCR_{infant} / ELCR_{mother} = 2.8 \times 10^{-4} / 2.3 \times 10^{-4} = 1.2$$

$$\text{Noncancer Relative Risk Ratio} = HQ_{infant} / HQ_{mother} = 317 / 13 = 24$$

This evaluation shows that the breast-feeding infant's excess lifetime cancer risk is slightly less than the calculated risk to the mother, and the non-cancer risk to the infant is 24 times greater than the non-cancer risk to the mother for PCB exposure. Although the example was performed using the fish ingestion pathway, **this result is independent of the exposure pathway or dose to the mother.** For PCBs, regardless of the exposure pathway to the mother or the dose, the excess lifetime cancer risk to the infant will always be approximately equal to the risk to the mother, and the hazard quotient to the infant will always be 24 times the hazard quotient to the mother. This assumes that the conditions used to derive the default values are met. The relative risk ratios are dependent on the metabolic half-life of the compound, and the difference between the subchronic and chronic reference doses. At a half-life greater than 60 days, the exposure to the infant will be greater than the exposure to the mother.

A relative risk ratio of 24 for PCBs is not unexpected. It is based on a dose to the infant 36 times the dose to the mother. Other estimates are that the PCB dose to the infant is

50 times the dose to the mother[5], so our calculated results are consistent with empirical studies.

Table 3 provides a summary of the relative risk ratios for infant/mother for the major bioaccumulating chemicals. This table provides a convenient method of including a breast-feeding pathway evaluation in risk assessments without having to perform the intermediate calculations. For any exposure pathway in a risk assessment where women (including girls) are exposed to bioaccumulating chemicals, the risk to infants from future breastfeeding can be calculated by multiplying the calculated excess lifetime cancer risk or hazard quotient by the factors shown in Table 3. Example calculations are shown in Table 4.

Comparison of Calculated Risks with Acceptable Levels

Using the approach presented in this appendix, the example excess lifetime cancer risk is approximately 3×10^{-4} for an infant consuming total PCBs in human milk for one year. This is substantially above the acceptable excess lifetime cancer risk of to 1×10^{-6}.

For non-cancer effects of PCB exposure, the calculated hazard quotient is 317. For hazard quotients above 1, unacceptable exposures may be occurring and there may be concern for potential non-cancer effects. Generally, the greater the magnitude of the hazard quotient above 1, the greater the level of concern for non-cancer health effects.

The calculated cancer risks and non-cancer hazards are based on a total PCB concentration in whole-body resident fish composites of 1 mg/kg. Although this concentration was used as a convenient value to demonstrate the calculations, it is within the range of total PCB concentrations measured in resident fish tissue at contaminated sites in Oregon. Because the calculated excess lifetime cancer risk and hazard quotient are considerably above acceptable levels, we conclude that infant exposure to chemicals in human milk will be an important pathway for sites contaminated with bioaccumulating chemicals.

UNCERTAINTY EVALUATION

Following standard guidance, the risk assessment for this pathway should include an evaluation of the associated uncertainties. During our evaluation of this pathway, we considered the following issues.

Exposure Assessment

The only exposure to infants evaluated was consumption of human milk. We did not consider other potential exposure routes, such as transplacental transfer of PCBs from mother to fetus during pregnancy.

Unlike Equation C-4, Equation C-5 does not rely on the assumption that intake to the mother has occurred for a period of time long enough relative to the half-life of the chemical that steady-state conditions are reached. For chemicals such as PCBs or CDDs/CDFs with half-lives on the order of 7 years, approximately 90 percent of steady-state concentration is reached after 21 years of exposure to the mother (3 half-lives). If

the mother is exposed for only 7 years prior to breast feeding, the concentration of chemical in milkfat will be only one-half the concentration calculated for steady-state conditions, and risks calculated using the steady-state equation (C-4) will be overestimated by a factor of 2.

We assumed that chemical concentrations in milkfat are equal to chemical concentrations in the mother's body fat. This may overestimate milkfat concentrations. However, EPA[1] considers this to be a reasonable assumption for lipophilic compounds, based on human data for CDDs/CDFs.

Comparison of Model Results with PBPK Models

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Toxicity Assessment

The ATSDR intermediate-duration MRL was derived from a study on monkeys that approximated exposure during breastfeeding using a mixture of PCB congeners typically found in human milk. The uncertainty factors were LOAEL to NOAEL conversion (10), sensitive members (10), and interspecies extrapolation (3), for a total of 300.

The chronic PCB RfD is also based on LOAELs developed from studies on monkeys. The health effects included inflammation of glands in the eye, distorted growth of finger and toe nails, and decreased antibody responses. The uncertainty factors used in the derivation of the human health RfD total 300, applied to an animal LOAEL of 0.005 mg/kg/day.

If a chronic RfD is used instead of a subchronic RfD, another uncertainty is the application of the RfD to one year of exposure, rather than long-term (lifetime) exposure. EPA's Superfund guidance defines chronic exposure as that between seven years and a lifetime. However, in its Combustion Guidance[2], EPA considered it appropriate to apply the chronic RfD to one year of exposure to human milk, at least for screening purposes. Application of the chronic RfD to one year of exposure may also be appropriate considering the potential sensitivity of infants to adverse health effects.

Risk Characterization

Using the chronic RfD for PCBs instead of the intermediate duration MRL, the calculated hazard quotient is:

$$HQ_{infant} = 0.0095 \text{ mg/kg/day} / 2 \times 10^{-5} \text{ mg/kg/day} = 475$$

The chronic HQ is 1.5 times the subchronic HQ of 317.

Body Burden Reductions

Incorporation of body burden reduction during a year of breast feeding was included in Equation C-4 for the first infant that is breast-fed. For additional infants that are breast-fed by the same woman, the mother's body burden will be reduced to about half of the

body burden prior to the previous breast-fed child. However, evaluation of infant risk should be based on the most exposed infant, which will almost always be the first-born child.

Relative Exposure

EPA considered presenting the potential risks from human milk consumption as a ratio to background risk rather than as an excess lifetime cancer risk or hazard quotient. Background total PCB concentrations reported in the literature include 0.27 mg/kg-lipid in milk[8], 0.32 mg/kg-lipid[9], and 0.38 mg/kg-lipid[10]. Using the assumed total PCB concentration of 1 mg/kg in fish tissue and the assumed fish consumption rate, the calculated total initial PCB concentration in human milk is 1.9 mg/kg-lipid. As an alternative presentation of risk in the uncertainty section, this result can be discussed as corresponding to a risk approximately 5 to 7 times that of background concentrations.

Fish Advisories

DEQ is aware that in some major rivers, consumption of resident fish by mothers who are breast feeding is already discouraged by fish advisories. For example, the Oregon Department of Human Services (DHS) advisory for PCBs in the Willamette River states that:

> Women of childbearing age, particularly pregnant or breastfeeding women, children and people with weak immune systems, thyroid or liver problems, should avoid eating resident fish from Portland Harbor, especially carp, bass and catfish.

For this reason, there may currently be limited infant exposure to human milk contaminated as a result of consumption of resident fish in the lower Willamette River. In addition, DHS advice on preparing fish for consumption, including removing fat from fillets (rather than consuming whole-body fish), could substantially lower risks to fish consumers, and also subsequently to breast-feeding infants. However, the results presented here appear to quantitatively support the advisory, and indicate that there are potentially significant unacceptable risks by the breast-feeding pathway.

HEALTH CONSULTATION ON BREAST-FEEDING PATHWAY

EPA asked the Oregon Environmental Health Assessment Program (EHAP, formerly SHINE) to develop recommendations on how to address the potential health risks for infants exposed to PCBs in human milk in the context of the many health benefits of breast-feeding. EHAP's evaluation and recommendations were reviewed by ATSDR, and are included in Attachment 1.

ENDNOTES

[1] EPA 1998. *Assessing Health Risks Associated with Multiple Pathways of Exposure to Combustor Emissions.* EPA 600/R-98/137, December 1998.
[2] EPA 2005. *Human Health Risk Assessment Protocol for Hazard Waste Combustion Facilities.* EPA 530-R-05-006, September 2005.
[3] EPA 1997. *Exposure Factors Handbook.* National Center for Environmental Assessment, Office of Research and Development. August 1997.
[4] EPA 2002. *Child-Specific Exposure Factors Handbook.* National Center for Environmental Assessment, Office of Research and Development. EPA-600-P-00-002B, Interim Report. September 2002.
[5] ATSDR 2000. *Toxicological Profile for Polychlorinated Biphenyls.* Agency for Toxic Substances and Disease Registry (Update, November 2000).
[6] Allan H. Smith. Infant Exposure Assessment for Breast Milk Dioxins and Furans Derived from Waste Incineration Emissions. *Risk Analysis*, Vol. 7, No. 3. 1987.
[7] EPA 2009. Risk and Technology Review (RTR). Risk Assessment Methodologies: For Review by the EPA's Science Advisory Board. EPA-452/R-09-006. June 2009.
[8] Greizerstein, H.B., C. Stinson, P. Mendola, G.M. Buck, P.J. Kostyniak, and J.E. Vena. 1999. Comparison of PCB congeners and pesticide levels between serum and milk from lactating women. *Environ. Res.* 80(3):280-6.
[9] Korrick, S. and L. Altschul. 1998. High breast milk levels of polychlorinated biphenyls (PCBs) among four women living adjacent to a PCB-contaminated waste site. E*nviron. Health Perspect.* 34 106:513.
[10] Noren, K. and D. Meironyte. 2000. Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20-30 years. *Chemosphere* 40:1111-23.

Table 1
Half-lives and Toxicity Values for Bioaccumulating Chemicals

Chemical	Half-life (days)	Oral RfDsubchronic (mg/kg/day)	Oral RfDchronic (mg/kg/day)	Oral Slope Factor $(mg/kg/day)^{-1}$
CDDs/CDFs TEQ	**2550**	**-**	**1×10^{-9}**	**1.3×10^{5}**
DDD	**120**	**-**	**-**	**0.24**
DDE	**120**	**-**	**-**	**0.34**
DDT	**120**	**-**	**5.0×10^{-4}**	**0.34**
Total PCB	**2550**	**3×10^{-5}**	**2×10^{-5}**	**2**
PCB TEQ	**2550**	**-**	**1×10^{-9}**	**1.3×10^{5}**

Notes:
Source of half-lives:
ATSDR 1977. Toxicological Profile for Chlorinated Dibenzo-p-dioxins. Draft for Public Comment. Agency for Toxic Substances and Disease Registry. September 1997.
ATSDR 2002. Toxicological Profile for DDT/DDD/DDE (Update). Agency for Toxic Substances and Disease Registry. September 2002.
ATSDR 2000. Toxicological Profile for Polychlorinated Biphenyls (Update). Agency for Toxic Substances and Disease Registry. November 2000.

Source of reference doses (RfDs) and oral slope factors (SFo):
EPA 2009. Regional Screening Levels.
www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

Source of subchronic RfD (taken from ATSDR Minimal Risk Level [MRL]):
ATSDR 2000. Toxicological Profile for Polychlorinated Biphenyls (Update). Agency for Toxic Substances and Disease Registry. November 2000.

Table 2
Parameters for Evaluation of Risk to Infant Consuming Human Milk Contaminated with PCBs

Parameter	Units	Description	Value[a]	Source
ADD_{mat}	mg/kg/day	Average daily dose to mother	Calculated	-
DAI_{mat}	mg/kg/day	Average daily absorbed dose to mother	Calculated	-
AE	unitless	Absorption efficiency of chemicals	1	EPA 1998
ADD_{infant}	mg/kg/day	Average daily dose to infant	Calculated	-
C_{fish}	mg/kg	Chemical concentration in fish	Calculated from site data. Example uses 1.	-
IR_{fish}	g/day	Ingestion rate of fish	17.5 (recreational fishers)	EPA 2000
CF	kg/g	Conversion factor	0.001	
F_{fish}	unitless	Fraction of fish contaminated	1	
BW_{mat}	kg	Body weight of mother (mean for ages 15 to 44)	66	EPA 2009
BW_{inf}	kg	Average body weight of infant over 1 year	7.8	EPA 1998
$C_{milkfat,ss}$	mg/kg-lipid	Steady state chemical concentration in milkfat prior to breastfeeding	Calculated	-
$C_{milkfat,avg}$	mg/kg-lipid	Average chemical concentration in milkfat during breastfeeding	Calculated	-
h	days	Half-life of chemical	Chemical-specific	
f_f	unitless	Fraction of ingested chemicals stored in fat	0.9	EPA 1998
f_{fm}	unitless	Fraction of mother's weight that is fat	0.3	EPA 1998
f_{mbm}	unitless	Fraction of human milk that is fat	0.04	EPA 1998
k_{elim}	$days^{-1}$	Elimination constant for chemical in non-lactating mother	Calculated	
k_{elac}	$days^{-1}$	Elimination constant for chemical in lactating mother	Calculated	

Table 2
Parameters for Evaluation of Risk from Consuming Human Milk

Parameter	Units	Description	Value[a]	Source
t_{pn}	days	Duration of mother's exposure prior to breastfeeding	20 years = 7300 days	Assumption
t_{bf}	days	Duration of breastfeeding	1 year = 365 days	EPA 1998
ED_{inf}	days	Exposure duration of breast-feeding child	1 year = 365 days	EPA 1998
CR_{milk}	kg/day	Average consumption rate of human milk	0.98 kg/day	EPA 2009
AT	days	Averaging time – carcinogen	70 years[c] = 25550 days	-
		Averaging time – non-carcinogen	= ED	-
ELCR	risk	Excess lifetime cancer risk	Calculated	-
HQ	hazard	Hazard quotient	Calculated	-
SF_o	$(mg/kg/day)^{-1}$	Cancer slope factor – oral	Table 1	-
RfD	(mg/kg/day)	Reference dose (chronic)	Table 1	-
MRL	(mg/kg/day)	Minimal risk level (intermediate duration)	Table 1	-

Notes:

a) Exposure assumptions taken from:
EPA 1997. *Exposure Factors Handbook*. Office of Research and Development, U.S. Environmental Protection Agency. (Update to EPA/600/P-96/002Babc, August 1997).

EPA 2000. *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)*. U.S. Environmental Protection Agency, Office of Water. EPA-822-B-00-004, October 2000.

EPA 2002. *Child-Specific Exposure Factors Handbook.* National Center for Environmental Assessment, Office of Research and Development. EPA-600-P-00-002B, Interim Report. September 2002.

EPA 2005. *Human Health Risk Assessment Protocol for Hazard Waste Combustion Facilities.* EPA 530-R-05-006. September 2005.

EPA 2009. Risk and Technology Review (RTR). Risk Assessment Methodologies: For Review by the EPA's Science Advisory Board. EPA-452/R-09-006. June 2009.

b) EPA combustion facilities guidance (EPA 2005) uses 1 year. We consider this too conservative, and use the lifetime AT_c value typically used at Superfund sites.

Table 3
Default Ratios for Calculating Human Milk Consumption Risks Based on Risks Calculated for Exposure to the Mother

Chemical	Ratio to Convert Chronic HQ for Mother to Subchronic HQ for Infant	Ratio to Convert ELCR for Mother to ELCR for Infant
CDDs/CDFs	**1.8**	**1.2**
DDT	**2.2**	**0.0073**
Total PCB	**24**	**1.2**
PCB TEQ	**1.8**	**1.2**

Notes:
HQ = hazard quotient
ELCR = excess lifetime cancer risk
CDD = chlorinated dibenzo-*p*-dioxin
CDF = chlorinated dibenzofuran
DDT = dichlorodiphenyltrichloroethane
PCB = polychlorinated biphenyl
TEQ = 2,3,7,8-tetrachlorodibenzo-*p*-dioxin toxicity equivalent

Table 4
Example Calculation of Human Milk Consumption Risks Based on Risks Calculated for Exposure to the Mother

	Hazard Quotient		Excess Lifetime Cancer Risk	
Chemical	**Adult**	**Infant[a]**	**Adult**	**Infant[a]**
Soil ingestion exposure pathway				
Arsenic	0.13	-	2×10^{-6}	-
Total PCB	0.38	6.8	7×10^{-6}	6×10^{-6}
PCB TEQ	-	-	5×10^{-6}	5×10^{-6}
CDD/CDF TEQ	-	-	1×10^{-6}	9×10^{-7}
Total TEQ	-	-	6×10^{-6}	5×10^{-6}
Total	**0.51**	**6.8**	**2×10^{-5}**	**1×10^{-5}**
Fish ingestion exposure pathway				
Total PCB	13	234	2×10^{-4}	2×10^{-4}
PCB TEQ	-	-	2×10^{-4}	2×10^{-4}
CDD/CDF TEQ	-	-	8×10^{-5}	7×10^{-5}
Total TEQ	-	-	3×10^{-4}	3×10^{-5}
Total	**13**	**234**	**5×10^{-4}**	**5×10^{-4}**
Total for all exposure pathways				
Total	**14**	**241**	**5×10^{-4}**	**5×10^{-4}**

Notes
a) Calculated using infant/mother risk ratios shown in Table 3.

Appendix C - Attachment 1

PCBs in Breast Milk at Portland Harbor

Letter from
Oregon Department of Human Services, Public Health Division
to
U.S. Environmental Protection Agency, Region 10
16 September 2008

Appendix C - Attachment 2

Consideration of Non-Steady State Chemical Concentrations in Milkfat and Loses During Breast Feeding

The EPA combustion facility guidance document[1] and ATSDR's Toxicological Profile[2] do not elaborate on the derivation of the equation for calculation of chemicals present in milkfat. The main EPA reference for the equation is Allan Smith's evaluation of infant exposure to chlorinated dibenzodioxins and chlorinated dibenzofurans in human milk[3]. In this attachment, we first explicitly derive the non-steady state equation used to approximate chemical concentrations in maternal body fat, which is assumed to be equivalent to the concentration in human milk. Then we consider chemical mass loses in the mother as a result of breast-feeding. Additional information on the derivation of Equation C-5 is presented in Appendix C of EPA's MPE Guidance[4].

Non-Steady State Chemical Concentration in Milkfat

The chemical body burden in the mother is calculated assuming first-order kinetics:

Equation C-11
General Body Burden Calculation

$$B_t = B_0 \, e^{-kt}$$

Where:
t = Time period (years)
B_t = Body burden at time t (mg)
B_0 = Body burden at time t = 0 (mg)
k = Rate constant (days^{-1})

Using this standard approach, the maternal daily chemical intake, m (mg/kg/day), is used to calculate the concentration of chemical in the mother's tissue. The maternal chemical concentration (C_{mother} in mg/kg-body-weight) at time T is:

$$C_{mother} = \int_0^T m e^{-kt} \, dt$$

where the mother is exposed to the chemical from time t = 0 to time $t = T$ (in days). The general solution to this equation is:

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[1] U. S. EPA. *Human Health Risk Assessment Protocol for Hazard Waste Combustion Facilities.* EPA 530-R-05-006, September 2005.
[2] ATSDR. *Toxicological Profile for Polychlorinated Biphenyls.* November 2000.
[3] Allan H. Smith. Infant Exposure Assessment for Breast Milk Dioxins and Furans Derived from Waste Incineration Emissions. *Risk Analysis,* Vol. 7, No. 3. 1987.
[4] EPA 1998. *Assessing Health Risks Associated with Multiple Pathways of Exposure to Combustor Emissions.* EPA 600/R-98/137, December 1998.

$$\int_0^T me^{-kt}\,dt = \frac{me^{-kT}}{-k} - \frac{me^{0}}{-k} = \frac{me^{-kT}}{-k} + \frac{m}{k} = \frac{m}{k}(1 - e^{-kT})$$

This results in the following equation, noting that the elimination rate constant k = k_{elim}:

Equation C-12
Chemical Concentration in Mother

$$C_{mother} = \frac{m}{k_{elim}}(1 - e^{-k_{elim}T})$$

Where
C_{mother} = Chemical concentration in mother at time T (days)
m = Absorbed chemical dose to mother (mg/kg/day)
k_{elim} = Elimination rate constant for non-lactating women ($days^{-1}$)
T = Time of exposure to mother before breastfeeding (days)

Equation C-12 is applicable to conditions that have not reached steady state. To derive the steady state equation, we will use the definition of k_{elim} in the main text to convert from elimination rate constant to chemical halflife.

Equation C-6
Biological Elimination Rate Constant for Women Prior to Breastfeeding

$$k_{elim} = \frac{\ln(2)}{h}$$

Where
k_{elim} = Elimination rate constant for non-lactating women ($days^{-1}$)
h = Half-life of chemical (days)

Using this relationship, Equation C-12 can be presented as:

Equation C-12A
Chemical Concentration in Mother (Version 2)

$$C_{mother} = \frac{mh}{\ln(2)}\left(1 - e^{\frac{-\ln(2)}{h}T}\right)$$

For exposure periods to the mother (T) that are long relative to the halflife of the chemical (h), ln(2)T/h becomes large, $e^{-\ln(2)T/h}$ becomes much less than 1, and $(1 - e^{-\ln(2)T/h})$ approaches a value of 1. At steady state:

Equation C-13
Steady State Chemical Concentration in the Mother

$$C_{mother} = \frac{mh}{\ln(2)}$$

Using the PCB example and Equation C-12A, if the exposure period of the mother to contaminated fish (*T*) is equal to the chemical half-life (*h*) of 7 years for PCBs, then the chemical concentration in the mother's tissue is:

$$C_{mother} = 0.5\frac{mh}{\ln(2)}$$

If the mother is exposed to PCBs for 7 years prior to breast-feeding, the PCB concentration in lipid tissue is one-half the value obtained assuming steady-state conditions.

If the exposure period of the mother to contaminated fish is equal to four half-lives (*T* = 4*h* = 28 years), then the chemical concentration in the mother's tissue is:

$$C_{mother} = 0.94\frac{mh}{\ln(2)}$$

Equation C-12 can be adjusted to make it a lipid-based concentration by considering the fraction of the chemical stored in fat tissue (f_f) and the fraction of the mother's weight that is fat (f_{fm}).

$$C_{mother} = \frac{mh}{\ln(2)}\frac{f_f}{f_{fm}}$$

Substituting the symbol DAI_{mat} for *m*, and assuming that the chemical concentration in milkfat is equivalent to the chemical concentration in the mother's fat tissue, yields the steady state equation for $C_{milkfat}$ shown in the main text as Equation C-4.

$$C_{milkfat} = \frac{DAI_{mat}\,h}{\ln(2)}\frac{f_f}{f_{fm}}$$

Or, alternatively, using the elimination rate constant instead of the chemical halflife:

Equation C-4A
Steady State Chemical Concentration in Milkfat (Version 2)

$$C_{milkfat} = \frac{DAI_{mat}}{k_{e\lim}}\frac{f_f}{f_{fm}}$$

To calculate non-steady state concentrations, a modified version of Equation C-12 can be used:

Equation C-14
Chemical Concentration in Milkfat Prior to Breastfeeding

$$C_{milkfat,pn} = \frac{DAI_{mat}}{k_{e\,\mathrm{lim}}} \frac{f_f}{f_{fm}} (1 - e^{-k_{elim} t_{pn}})$$

Where:

$C_{milkfat,pn}$ = Chemical concentration in milkfat prior to breastfeeding (mg/kg-lipid)
DAI_{mat} = Daily absorbed chemical intake to mother (mg/kg/day); Equation C-2
f_f = Fraction of ingested chemical stored in fat (0.9)
f_{fm} = Fraction of mother's weight that is fat (0.3 kg-lipidBW/kg-totalBW)
k_{elim} = Elimination rate constant for non-lactating women; Equation C-6
t_{pn} = Duration of mother's exposure prior to breastfeeding (days)

Using Equation C-4 for the steady state concentration in milkfat, $C_{milkfat,ss}$, Equation C-14 can be modified to express $C_{milkfat,pn}$ in terms of $C_{milkfat,ss}$.

Equation C-14A
Chemical Concentration in Milkfat Prior to Breastfeeding (Version 2)

$$C_{milkfat,pn} = C_{milkfat,ss} (1 - e^{-k_{elim} t_{pn}})$$

Reduction in Chemical Dose to Infant Over Time

The loss of chemical mass through breast-feeding will reduce the chemical body burden in the mother, thereby reducing breast milk concentrations and dose to the infant over time. Equation C-5 accounts for reduction in chemical concentrations over time by including the rate constant k_{elac} for elimination of chemicals in milkfat. Because Equation C-5 is complex, it is difficult to determine the impact of reducing dose to the infant during the breastfeeding period. In this section, we look specifically at the reduction in chemical concentration in human milk over time to determine the magnitude of this effect on the dose to the infant.

One of the reasons Equation C-5 is complex is because it assumes that the mother continues to be exposed to chemicals during lactation. We make the simplifying assumption that the mother ceases to be exposed to chemicals during breastfeeding. Because the default breastfeeding period of 1 year is short relative to the default exposure duration of the mother before breastfeeding (20 years), this assumption should have little impact on the average chemical concentration in milk.

With this simplifying assumption, the reduction in chemical concentration in milkfat can be approximated by the following equation based on Equation C-11.

Equation C-15
Chemical Concentration in Milkfat

$$C_{milkfat,t} = C_{milkfat,pn} e^{-kt}$$

Where
$C_{milkfat,t}$ = Chemical conc. in milkfat during breastfeeding at time t (mg/kg-lipid)
$C_{milkfat,pn}$ = Chemical concentration in milkfat prior to breastfeeding (mg/kg-lipid)
k = Elimination rate constant for lactating women ($days^{-1}$)
t = Duration of lactation (days)

The average chemical concentration in milkfat during lactation is:

Equation C-16
Average Chemical Concentration in Milkfat

$$C_{milkfat,avg} = \frac{1}{T}\int_0^T C_{milkfat,pn}\, e^{-kt} dt$$

Where
$C_{milkfat,avg}$ = Average chemical conc. in milkfat during breastfeeding (mg/kg-lipid)
$C_{milkfat,pn}$ = Chemical concentration in milkfat prior to breastfeeding (mg/kg-lipid)
k = Elimination rate constant for lactating women ($days^{-1}$)
T = Duration of lactation (days)

Using modified nomenclature, considering that all concentrations are for milkfat, the general solution to this equation is:

$$C_{avg} = \frac{1}{T}\int_0^T C_{pn}\, e^{-kt} dt = \frac{C_{pn}}{T}\int_0^T e^{-kt} dt = \frac{C_{pn}}{T}\left(\frac{e^{-kT}}{-k} - \frac{e^{-k(0)}}{-k}\right) = \frac{C_{pn}}{T}\left(\frac{e^{-kT}}{-k} - \frac{1}{-k}\right)$$
$$= \frac{C_{pn}}{kT}\left(1 - e^{-kT}\right) = C_{pn}\left(\frac{1 - e^{-kT}}{kT}\right)$$

This simplified equation shows that the average chemical concentration in milkfat can be approximated by the chemical concentration in milkfat prior to lactation (C_{pn}) times the factor $(1 - e^{-kT})/kT$ to account for loss of chemical mass during breastfeeding.

Using Equation C-14A for C_{pn}, the above equation can be modified so that the average chemical concentration in milkfat over the duration of breastfeeding can be expressed in terms of the steady state concentration in the mother:

Equation C-17
Average Chemical Concentration in Milkfat as a Function of the Steady State Concentration in the Mother

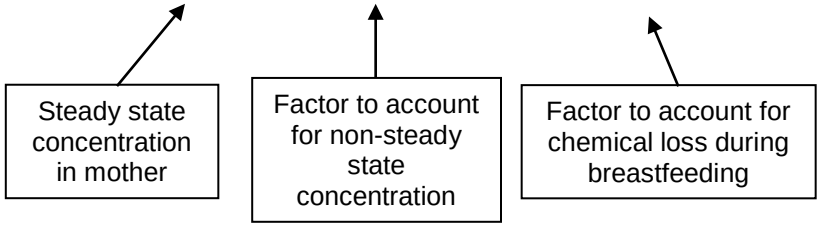
$$C_{milkfat,avg} = C_{milkfat,ss}\left(1 - e^{-k_{elim} t_{pn}}\right)\left(\frac{1 - e^{-k_{elac} t_{bf}}}{k_{elac} t_{bf}}\right)$$

where

$C_{milkfat,avg}$ = Average chemical conc. in milkfat during breastfeeding (mg/kg-lipid)
$C_{milkfat,ss}$ = Steady state chemical concentration in milkfat prior to breastfeeding (mg/kg-lipid)
k_{elim} = Elimination rate constant prior to lactation ($days^{-1}$)
k_{elac} = Elimination rate constant during lactation ($days^{-1}$)
t_{pn} = Duration of exposure to mother prior to breastfeeding ($days^{-1}$)
t_{bf} = Duration of exposure to infant during breastfeeding ($days^{-1}$)

The PCB example can be used to show the relative impact resulting from considering non-steady state chemical concentrations in the mother, and chemical mass loss during breastfeeding.

$$C_{milkfat,avg} = C_{milkfat,ss}\left(1 - e^{-k_{elim}t_{pn}}\right)\left(\frac{1 - e^{-k_{elac}t_{bf}}}{k_{elac}t_{bf}}\right)$$



In the PCB example, the factor for non-steady state concentration is 0.86, and the factor for chemical loss during breastfeeding is 0.70, so

$$C_{avg} = C_{ss} \times 0.86 \times 0.70 = C_{ss} \times 0.61$$

Collectively, consideration of these two factors reduces the estimate of average PCB concentration in milkfat by about 40 percent.

The lower the half-life of the chemical relative to the exposure period of the mother, the less accurate this approximation of average chemical concentration in milkfat will be.